

Appln. No. 09/982,095  
Amd. dated April 28, 2005  
Reply to Office Action of November 2, 2004

**Amendments to the Claims**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1(Currently amended). A method for screening and identifying molecules that mediate neuronal cell survival in the absence of neurotrophic factors and transactivate a neurotrophin neurotrophic receptor and mediate neuronal cell survival in the absence of neurotrophins, comprising assay A or assay A in combination with either or both of assay B and assay C, wherein:

assay A comprises:

treating neuronal cells with a candidate small molecule activator;

reacting ~~[[a]]~~ the neurotrophic receptor, obtained from a cell lysate of the treated ~~neuronal~~ cells, with an anti-phosphotyrosine antibody specific for ~~[[a]]~~ the phosphorylated form of the ~~neurotrophin~~ neurotrophic receptor; and

detecting ~~specific~~ binding of the anti-phosphotyrosine antibody to a phosphorylated form of the ~~neurotrophin~~ neurotrophic receptor to identify a small molecule ~~activator~~ transactivator of the ~~neurotrophin~~ neurotrophic receptor that mediates neuronal cell survival in the absence of neurotrophins by transactivating the neurotrophic receptor;

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assay B comprises:

treating neuronal cells with a candidate small molecule  
~~activator~~ transactivator;

reacting either phosphatidylinositol 3'-kinase (PI3-K),  
obtained from a cell lysate of the treated neuronal cells, with  
an anti-phospho-PI3-K antibody specific for the phosphorylated  
form of PI3-K or Akt, obtained from a cell lysate of the treated  
neuronal cells, with an anti-phospho-Akt antibody specific for  
the phosphorylated form of Akt; and

detecting ~~specific~~ binding of the anti-phospho-PI3-K  
antibody to the phosphorylated form of PI3-K or binding of the  
anti-phospho-Akt antibody to the phosphorylated form of Akt to  
identify a small molecule ~~activator of a neurotrophin~~  
transactivator of the neurotrophic receptor and its downstream  
Akt target; and

assay C comprises:

culturing neuronal cells in the presence of  
~~neurotrophins~~ neurotrophic factors;

treating and culturing the neuronal cells with a  
candidate small molecule ~~activator~~ transactivator in the absence  
of ~~neurotrophins~~ neurotrophic factors; and

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determining the level of cell survival to identify a small molecule ~~activator of the neurotrophin~~ transactivator of the neurotrophic receptor.

2(Currently amended). The method of claim 1, wherein the ~~neurotrophin~~ neurotrophic receptor is a Trk receptor.

3(Original). The method of claim 2, wherein the Trk receptor is TrkA receptor.

4(Original). The method of claim 3, wherein the neuronal cells are PC12 neuronal cells.

Claim 5 (Cancelled).

6(Currently amended). The method of claim 1, wherein the candidate small molecule ~~activator~~ transactivator is a ligand of a G protein coupled receptor (GPCR).

7(Currently amended). The method of claim 1, wherein the ~~neurotrophin~~ neurotrophic receptor is a Ret receptor.

8(Original). The method of claim 7, wherein the neuronal cells are N2a neuroblastoma cells.

9(Original). The method of claim 1, wherein, in the reacting and detecting steps of assay B, Akt is reacted with anti-phospho-Akt antibody and specific binding of anti-phospho-Akt antibody to the phosphorylated form of Akt is detected.

10(Original). The method of claim 9, wherein assay B further comprises:

reacting Akt, obtained from a cell lysate of the treated neuronal cells, with an anti-Akt antibody; and

detecting specific binding of the anti-Akt antibody to Akt to provide an assessment of the relative level of phosphophosylated Akt and the extent of activation.

11(Original). The method of claim 1, wherein in the reacting and detecting steps of assay B, PI3-K is reacted with anti-phospho-PI3-K antibody and specific binding of anti-phospho-PI3-K antibody to the phosphorylated form of PI3-K is detected.

12(Currently amended). The method of claim 11, wherein assay B further comprises:

reacting PI3-K, obtained from a cell lysate of the treated neuronal cells, with an anti-PI3-K antibody; and

detecting ~~specific~~ binding of the anti-PI3-K antibody to PI3-K to provide an assessment of the relative level of phosphophosylated PI3-K and the extent of activation.